RESEARCH PAPER

Nephroprotective and Antioxidant Potential of the Methanolic Extract of *Gloriosa superba* Against Paracetamol-Induced Renal Damage in Wistar Rats: A Biochemical and Histopathological Study

Sakina Alavi[1], Dr. Mehta Parulben D.[1], Dr. Rita Mourya[2]

1. SAM College of Pharmacy, Faculty of Medical and Paramedical Sciences, SAM Global University Raisen-(MadhyaPradesh) India- 464551

2 School of Pharmacy, Faculty of Medical and Paramedical Sciences, SAM Global University Raisen-(MadhyaPradesh) India- 464551

Abstract

Background: Paracetamol (PCM) overdose is a well-recognised cause of drug-induced nephrotoxicity, mediated largely through reactive-metabolite formation and oxidative stress. *Gloriosa superba* L. (Colchicaceae) is a traditionally valued medicinal plant rich in antioxidant phytoconstituents. **Objective:** To evaluate the phytochemical profile, in-vitro antioxidant capacity and in-vivo nephroprotective activity of the methanolic extract of *Gloriosa superba* (MEGS) against PCM-induced renal injury in Wistar rats. **Methods:** Successive extraction was performed with petroleum ether and methanol. The methanolic extract was subjected to qualitative and quantitative phytochemical screening, total phenolic (TPC) and flavonoid (TFC) estimation, and DPPH radical-scavenging assay. Acute oral toxicity was assessed as per OECD 423. Nephrotoxicity was induced with PCM (500 mg/kg, p.o.) for 14 days; animals were treated with silymarin (100 mg/kg) or MEGS (200 and 400 mg/kg). Urine volume, body weight, serum creatinine, blood urea nitrogen (BUN) and renal histopathology were evaluated. **Results:** Methanol gave a markedly higher yield (9.076%) than petroleum ether (2.085%) and was rich in alkaloids, flavonoids, tannins, glycosides and phenolics. TPC and TFC were 40.971 mg GAE/g and 29.419 mg RE/g, respectively; the extract showed concentration-dependent DPPH scavenging (IC_{50} = 40.029 µg/mL). MEGS was safe up to 2000 mg/kg. PCM significantly reduced urine output and body weight and elevated serum creatinine and BUN. MEGS restored these parameters in a dose-dependent manner, the 400 mg/kg dose producing near-normalisation comparable with silymarin, and preserved renal architecture on histopathology. **Conclusion:** MEGS possesses significant, dose-dependent nephroprotective activity against PCM-induced renal damage, most plausibly attributable to its phenolic and flavonoid-mediated antioxidant action.

Keywords: *Gloriosa superba*; nephroprotection; paracetamol-induced nephrotoxicity; oxidative stress; flavonoids; DPPH assay; Wistar rats.

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1. Introduction

Medicinal plants continue to represent a vital reservoir of therapeutic agents, providing raw material for a large proportion of drugs used in modern healthcare. Their sustained relevance stems from potent pharmacological efficacy, favourable safety profiles and economic accessibility, particularly in resource-limited settings. Plant-derived secondary metabolites such as alkaloids, flavonoids, tannins and phenolic acids underlie many of these activities, chiefly through their capacity to neutralise free radicals and modulate inflammatory pathways [1,2].

The kidney is a principal target organ for xenobiotic-induced injury because of its high blood flow, active tubular transport and its role in the concentration and excretion of toxic metabolites. Acute kidney injury (AKI) is characterised by an abrupt decline in renal function reflected by rising serum creatinine and falling urine output, and is a recognised risk factor for progression to chronic kidney disease [3,4]. Drugs account for a substantial share of nephrotoxic events, and their mechanisms include altered glomerular haemodynamics, direct tubular-cell toxicity, inflammation, crystal nephropathy and oxidative injury [5,6].

Paracetamol (acetaminophen, PCM) is among the most widely consumed analgesic–antipyretic agents. Although safe at therapeutic doses, overdose saturates its conjugation pathways and diverts metabolism toward cytochrome-P450-mediated formation of the reactive intermediate N-acetyl-p-benzoquinoneimine (NAPQI). Depletion of renal glutathione by NAPQI provokes lipid peroxidation, mitochondrial dysfunction and tubular necrosis, establishing PCM as a reliable experimental model of oxidative-stress-mediated nephrotoxicity [7,8]. Serum creatinine and blood urea nitrogen (BUN) remain the most accessible biochemical indicators of the resulting functional impairment [9].

Gloriosa superba L. (Colchicaceae), commonly known as the glory lily or flame lily, is a perennial

climber distributed across tropical Africa and Asia, including the Indian subcontinent. It is traditionally employed for its anti-inflammatory, analgesic, antimicrobial, anthelmintic and wound-healing properties and is an important industrial source of colchicine [10,11]. Previous reports have documented its antioxidant, antiulcer and antitumour activities, attributes broadly linked to its flavonoid, phenolic and alkaloid content [12,13]. Despite this pharmacological breadth, the protective potential of *G. superba* against drug-induced renal injury has not been systematically characterised.

Accordingly, the present study was designed to determine the phytochemical composition and in-vitro antioxidant capacity of the methanolic extract of *Gloriosa superba* (MEGS) and to evaluate its nephroprotective efficacy against PCM-induced renal damage in Wistar rats, using biochemical markers, general physiological indices and histopathological assessment, with silymarin as the reference standard.

2. Materials and Methods

2.1 Chemicals and reagents

Paracetamol was procured from Yarrow Chem Products (Mumbai, India). Analytical-grade methanol, ethanol, petroleum ether, sodium hydroxide, hydrochloric acid, sodium nitrite, aluminium chloride, Folin–Ciocalteu reagent, gallic acid, rutin and 1,1-diphenyl-2-picrylhydrazyl (DPPH) were obtained from Merck Life Science, HiMedia, SRL and Sigma-Aldrich (India). Silymarin was used as the standard nephroprotective agent, and commercial Erba diagnostic kits were used for biochemical estimations. All reagents were of analytical grade.

2.2 Collection and authentication of plant material

Fresh flowers of *Gloriosa superba* were collected from the local region of Bhopal, Madhya Pradesh, India, and authenticated by a qualified botanist. The material was washed, shade-dried at room temperature for approximately two weeks, mechanically pulverised into a coarse powder, passed through a No. 40 sieve and stored in airtight containers until extraction.

2.3 Extraction and determination of percentage yield

The powdered material was first defatted with petroleum ether and then extracted successively with methanol using a Soxhlet apparatus. Each extract was concentrated under reduced pressure in a rotary evaporator and stored at 4–8 °C. The percentage yield was calculated as: % yield = (weight of dried extract / weight of plant material taken) × 100 [14].

2.4 Qualitative phytochemical screening

Both extracts were screened for major secondary metabolites using standard chemical tests, including Dragendorff's test (alkaloids), ferric chloride test (tannins), Shinoda test (flavonoids), Salkowski test (steroids/terpenoids), Benedict's test (carbohydrates), Borntrager's test (glycosides), saponification test (fats and fixed oils), the foam test (saponins) and the bromine-water test (free sugars) [15].

2.5 Quantitative estimation of phytoconstituents

Total phenolic content (TPC) was determined by the Folin–Ciocalteu method. Extract or gallic-acid standard (0.5 mL) was mixed with 2 mL Folin–Ciocalteu reagent (1:10) and 4 mL sodium carbonate, incubated for 30 min, and absorbance recorded at 765 nm. TPC was expressed as mg gallic-acid equivalents per gram (mg GAE/g) [16]. **Total flavonoid content (TFC)** was estimated by the aluminium-chloride colorimetric method against a rutin standard, with absorbance measured at 510 nm and expressed as mg rutin equivalents per gram (mg RE/g) [17].

2.6 In-vitro antioxidant (DPPH) assay

Free-radical-scavenging activity was assessed using the DPPH assay. Test solutions (10–100 µg/mL) were mixed with 0.1 mM methanolic DPPH, incubated in the dark for 10 min, and absorbance measured at 515 nm against ascorbic acid as the reference standard. Percentage inhibition was calculated as [(A_control − A_sample)/A_control] × 100, and IC_{50} values were derived from the regression equations [18].

2.7 Experimental animals

Healthy adult male Wistar rats (250 ± 60 g) were housed under standard conditions (22 ± 2 °C, 12-h light/dark cycle) with free access to a standard pellet diet and water. All procedures were approved by the Institutional Animal Ethics Committee (IAEC) and conducted in accordance with CPCSEA guidelines.

2.8 Acute oral toxicity study

Acute oral toxicity was evaluated following OECD guideline 423 (acute toxic-class method). The extract was administered orally at 5, 50, 300 and 2000 mg/kg body weight, and animals were observed for behavioural, autonomic and physiological changes and mortality over 14 days [19].

2.9 Experimental design for nephroprotective evaluation

Thirty rats were randomly allocated to five groups (n = 6) and treated orally for 14 consecutive days:

Group I — Normal control (distilled water, 10 mL/kg);
Group II — Disease control (paracetamol, 500 mg/kg);
Group III — Standard (silymarin 100 mg/kg + PCM);
Group IV — MEGS 200 mg/kg + PCM;
Group V — MEGS 400 mg/kg + PCM.

On day 15, after an overnight fast, animals were anaesthetised with diethyl ether and blood was collected for serum separation. The 24-h urine sample was collected (day 14–15) using metabolic cages, and kidneys were excised for histopathology [20].

2.10 Biochemical and general parameters

Body weight was recorded on days 0, 7 and 14. Twenty-four-hour urine volume was measured. Serum creatinine and BUN were estimated using an automated biochemical analyser with commercial diagnostic kits following the manufacturer's protocols [21,22].

2.11 Histopathological examination

Excised kidneys were fixed in 10% neutral-buffered formalin, dehydrated, embedded in paraffin, sectioned at 4–5 µm and stained with haematoxylin and eosin. Sections were examined by light microscopy for tubular necrosis, glomerular degeneration and inflammatory-cell infiltration, and findings were compared across groups [23].

2.12 Statistical analysis

Data are expressed as mean ± SEM. Differences between groups were analysed by one-way analysis of variance (ANOVA) followed by Dunnett's multiple-comparison test, with $p < 0.05$ considered statistically significant.

3. Results

3.1 Extractive yield

The methanolic extract gave a substantially higher yield (9.076%) than the petroleum-ether extract (2.085%), indicating that the polar solvent extracted a broader range of phytoconstituents from the plant material (Table 1).

Solvent	Weight of material (g)	Extract obtained (g)	% Yield
Petroleum ether	175	3.65	2.085
Methanol	170	15.43	9.076

Table 1. Percentage yield of successive Gloriosa superba flower extracts.

3.2 Qualitative phytochemical screening

Preliminary screening revealed a markedly richer phytochemical profile for the methanolic extract, which contained alkaloids, tannins, flavonoids, fats and fixed oils, carbohydrates, glycosides, saponins and free sugars. The petroleum-ether extract contained only steroids/terpenoids and saponins, consistent with its non-polar, lipophilic character (Table 2). The presence of flavonoids, phenolic tannins and alkaloids in the methanolic extract supports its potential antioxidant and pharmacological activity.

Phytoconstituent (test)	Petroleum ether	Methanol
Alkaloids (Dragendorff's)	–	+
Tannins (ferric chloride)	–	+
Flavonoids (Shinoda)	–	+
Fats and fixed oils (saponification)	–	+
Steroids and terpenoids (Salkowski)	+	+
Carbohydrates (Benedict's)	–	+
Glycosides (Borntrager's)	–	+
Saponins (foam test)	+	+
Free sugars (bromine water)	–	+

Table 2. Preliminary qualitative phytochemical screening of Gloriosa superba extracts (+ present; – absent).

3.3 Total phenolic and flavonoid content

Using the gallic-acid and rutin calibration curves (Figures 1 and 2), the methanolic extract was found to contain a high total phenolic content of 40.971 mg GAE/g and a total flavonoid content of 29.419 mg RE/g (Table 3). Both calibration curves were highly linear ($R^2 > 0.997$), and the low standard deviations of the extract absorbance values confirm good analytical reproducibility.

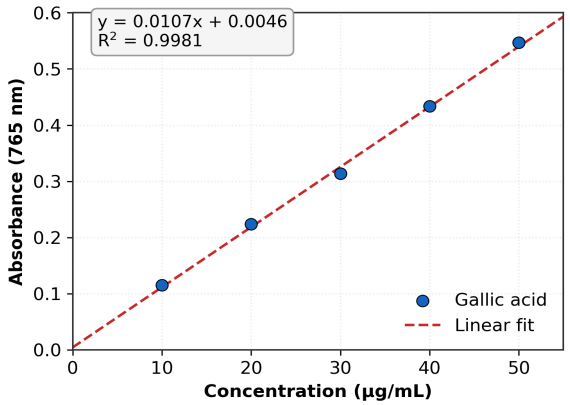

Figure 1. Gallic-acid standard calibration curve used for total phenolic-content estimation.

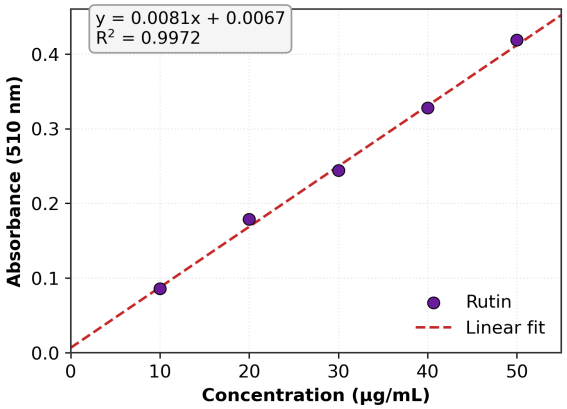

Figure 2. Rutin standard calibration curve used for total flavonoid-content estimation.

Parameter	Absorbance (mean ± SD)	Content
Total phenolic content (TPC)	0.443 ± 0.007	40.971 mg GAE/g
Total flavonoid content (TFC)	0.254 ± 0.011	29.419 mg RE/g

Table 3. Total phenolic and flavonoid content of the methanolic extract of Gloriosa superba.

3.4 In-vitro antioxidant activity

Both ascorbic acid and MEGS produced a concentration-dependent increase in DPPH radical-scavenging activity (Table 4, Figure 3). Ascorbic acid showed inhibition rising from 43.679% (10 µg/mL) to 75.025% (50 µg/mL) with an IC_{50} of 17.747 µg/mL, whereas the extract achieved 37.615–67.420% inhibition over 20–100 µg/mL with an IC_{50} of 40.029 µg/mL. Although lower than the standard, this represents appreciable antioxidant capacity consistent with the extract's phenolic and flavonoid content.

Concentration (µg/mL)	Ascorbic acid (% inhibition)	MEGS (% inhibition)
10	43.679	—
20	52.209	37.615
30	59.506	—
40	67.112	44.912
50	75.025	—
60	—	51.901
80	—	60.637
100	—	67.420
IC_{50} (µg/mL)	**17.747**	**40.029**

Table 4. DPPH radical-scavenging activity of ascorbic acid and the methanolic extract of Gloriosa superba (MEGS).

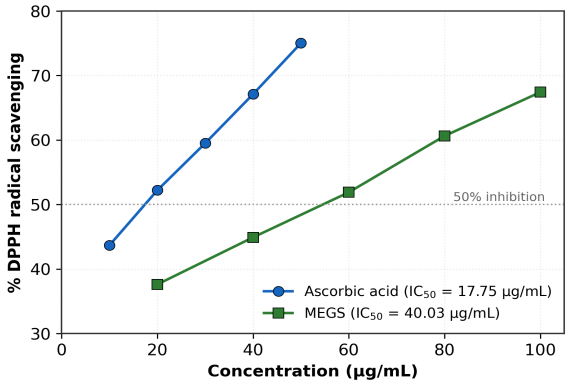

Figure 3. Concentration-dependent DPPH radical-scavenging activity of ascorbic acid and MEGS.

3.5 Acute oral toxicity

No mortality was recorded at any dose up to 2000 mg/kg. Minor, transient signs (mild salivation, lethargy and, at higher doses, occasional tremors and diarrhoea) were observed but resolved without lethality (Table 5). The extract was therefore considered safe, and 200 and 400 mg/kg were selected as the therapeutic doses for the nephroprotective study.

Observation	5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
Behaviour	N	N	N	L
Skin / eye / mucous membrane	N	N	N	N
Salivation	N	L	L	L
Lethargy	N	L	L	L
Sleep	N	N	N	L
Convulsions	N	N	L	L
Tremors	N	N	L	L
Diarrhoea	N	N	L	L
Morbidity	N	N	N	L
Mortality	**Nil**	**Nil**	**Nil**	**Nil**

Table 5. Acute oral toxicity observations for the Gloriosa superba extract (N = normal; L = low/mild effect).

3.6 Effect on urine volume

PCM markedly reduced 24-h urine output in the disease control group (1.052 ± 0.007 mL) relative to normal control (3.456 ± 0.003 mL), indicating impaired renal function. Silymarin restored output to 2.892 ± 0.016 mL, while MEGS improved urine volume dose-dependently, with the 400 mg/kg dose (2.459 ± 0.008 mL) markedly more effective than 200 mg/kg (1.663 ± 0.011 mL) (Table 6, Figure 4).

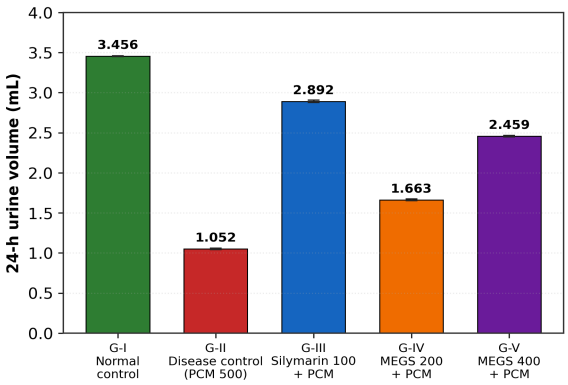

Figure 4. Effect of MEGS on 24-h urine volume in PCM-treated rats (mean ± SEM, n = 6).

3.7 Effect on body weight

The normal control group gained weight steadily, whereas the disease control group lost weight sharply (204.422 ± 3.394 g to 152.327 ± 4.621 g) over the study, reflecting PCM-induced systemic toxicity. Silymarin and both MEGS doses attenuated this loss, the 400 mg/kg group most closely approximating normal growth (Table 6, Figure 5).

Group	Day 0 (g)	Day 7 (g)	Day 14 (g)
I — Normal control	187.96 ± 5.42	194.51 ± 2.85	199.44 ± 3.86
II — Disease control (PCM)	204.42 ± 3.39	176.06 ± 4.93	152.33 ± 4.62
III — Silymarin + PCM	196.53 ± 4.30	184.52 ± 6.33	192.37 ± 2.54
IV — MEGS 200 + PCM	193.43 ± 2.74	175.43 ± 3.65	184.32 ± 6.42
V — MEGS 400 + PCM	208.52 ± 3.76	197.42 ± 5.65	202.52 ± 3.73

Table 6. Effect of MEGS on body weight (g) of PCM-treated rats (mean ± SEM, n = 6).

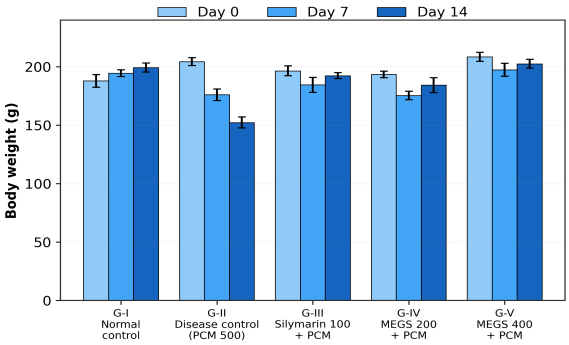

Figure 5. Body-weight profile across the 14-day study period.

3.8 Effect on serum creatinine and blood urea nitrogen

PCM significantly elevated serum creatinine (1.84 ± 0.011 mg/dL) and BUN (49.43 ± 0.004 mg/dL) compared with normal control (0.65 ± 0.006 and 19.056 ± 0.007 mg/dL, respectively), confirming renal dysfunction. Treatment with silymarin and MEGS produced a dose-dependent reduction in both markers. At 400 mg/kg, MEGS lowered creatinine to 0.93 ± 0.006 mg/dL and BUN to 31.39 ± 0.005 mg/dL, approaching the standard-drug response (Table 7, Figures 6 and 7).

Group	Serum creatinine (mg/dL)	BUN (mg/dL)
I — Normal control	0.65 ± 0.006	19.056 ± 0.007
II — Disease control (PCM)	1.84 ± 0.011	49.43 ± 0.004
III — Silymarin + PCM	0.86 ± 0.013	27.54 ± 0.009
IV — MEGS 200 + PCM	1.23 ± 0.009	38.53 ± 0.013
V — MEGS 400 + PCM	0.93 ± 0.006	31.39 ± 0.005

Table 7. Effect of MEGS on serum creatinine and BUN in PCM-treated rats (mean ± SEM, n = 6).

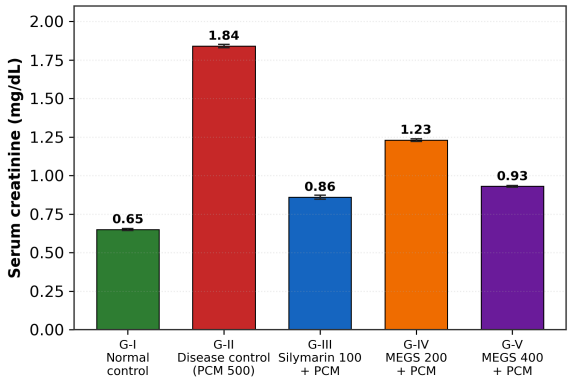

Figure 6. Effect of MEGS on serum creatinine levels.

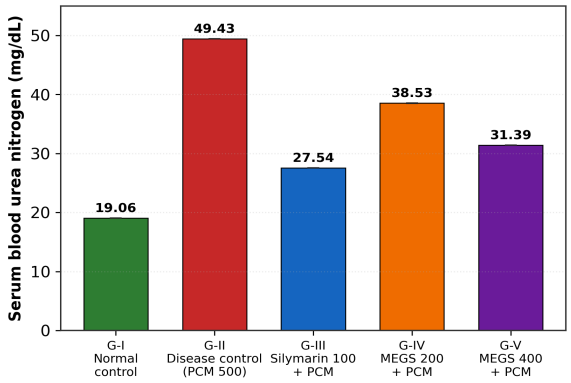

Figure 7. Effect of MEGS on serum blood urea nitrogen (BUN) levels.

3.9 Histopathological findings

Kidney sections from the normal control group displayed intact glomeruli, well-defined tubular architecture and normal renal corpuscles. The disease control group exhibited pronounced tubular necrosis, glomerular degeneration and inflammatory-cell infiltration, characteristic of PCM-induced nephrotoxicity. The silymarin group showed near-normal histology with preserved glomerular and tubular structures. MEGS at 200 mg/kg afforded only partial protection, with residual tubular degeneration and mild inflammation, whereas the 400 mg/kg dose produced marked restoration of renal architecture with reduced necrosis and inflammation. These structural findings corroborate the biochemical results and confirm a dose-dependent nephroprotective effect.

4. Discussion

The present study demonstrates that the methanolic extract of *Gloriosa superba* confers dose-dependent protection against PCM-induced nephrotoxicity in Wistar rats. The superior yield of the methanolic extract, together with its diverse phytochemical profile, is consistent with the higher polarity of methanol and its efficiency in recovering phenolic and flavonoid constituents, which were quantified at 40.971 mg GAE/g and 29.419 mg RE/g, respectively.

PCM nephrotoxicity is driven by the reactive metabolite NAPQI, which depletes glutathione, promotes lipid peroxidation and precipitates tubular necrosis. The resulting functional impairment manifests as reduced glomerular filtration, decreased urine output and accumulation of nitrogenous waste, reflected here by elevated serum creatinine and BUN and by loss of body weight in the disease control group [7,8]. The reversal of these changes by MEGS indicates preservation of glomerular filtration and tubular integrity.

The observed antioxidant capacity in the DPPH assay (IC_{50} = 40.029 µg/mL) provides a mechanistic basis for this protection. Phenolics and flavonoids scavenge reactive oxygen species by donating hydrogen atoms or electrons, chelate transition metals and inhibit lipid peroxidation, thereby attenuating oxidative renal injury. The correlation between the extract's phytochemical richness, its radical-scavenging activity and the degree of functional and structural recovery supports an antioxidant-mediated mechanism [1,18].

These findings are in agreement with earlier reports in which polyphenol-rich botanical extracts protected against nephrotoxicity induced by PCM or other agents. Extracts of *Annona squamosa* and *Eurycoma longifolia* have been shown to counter PCM-induced renal injury through antioxidant restoration [24,25], while *Glycyrrhiza glabra*, *Costus spicatus*, *Cinnamomum zeylanicum* and *Sambucus nigra* have demonstrated nephroprotection against cisplatin- or gentamicin-induced damage, attributed to combined antioxidant and anti-inflammatory actions [26,27,28,29]. The comparable, dose-dependent efficacy of MEGS reinforces the therapeutic value of phenolic/flavonoid-bearing plants in renal protection.

The near-normalisation of biochemical and histological parameters at 400 mg/kg—approaching, though not exceeding, the silymarin response—suggests that MEGS acts through mechanisms overlapping with those of the standard, principally the mitigation of oxidative stress. The favourable acute-toxicity profile (no mortality up to 2000 mg/kg) further supports its suitability for continued preclinical development.

Certain limitations should be acknowledged. The study did not directly quantify renal tissue oxidative-stress markers (e.g., malondialdehyde, reduced glutathione, catalase, superoxide dismutase) or inflammatory and apoptotic mediators, which would strengthen the mechanistic interpretation. Given the recognised toxicity of colchicine-bearing *G. superba*, future work should also isolate and characterise the responsible bioactive constituents and define a precise therapeutic window before any translational consideration.

5. Conclusion

The methanolic extract of *Gloriosa superba* possesses significant, dose-dependent nephroprotective activity against paracetamol-induced renal damage in Wistar rats. Protection was evidenced by restoration of urine output and body weight, normalisation of serum creatinine and BUN, and preservation of renal histoarchitecture, with the 400 mg/kg dose performing comparably to silymarin. The effect is most plausibly attributable to the antioxidant action of the extract's phenolic and flavonoid constituents. These results position *G. superba* as a promising candidate for the development of natural nephroprotective agents and warrant further studies to isolate the active principles, elucidate the underlying molecular mechanisms and establish safety margins.

Declarations

Ethics approval: All animal experiments were approved by the Institutional Animal Ethics Committee (IAEC) and performed in accordance with CPCSEA guidelines.

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Conflict of interest: The authors declare no conflict of interest.

Author contributions: All authors contributed to the study design, experimental work, data analysis and manuscript preparation, and approved the final version.

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